

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Originally Presented) A method for regulating the expression of a transgene of interest *in vivo* comprising:
 - simultaneously introducing into a target nonhuman animal tissue or cell a first nucleic acid comprising the sequence of a transgene of interest encoding a transcript of interest, and a second nucleic acid comprising the sequence of an inhibitory transgene encoding an inhibitory transcript specific for the transcript of interest, wherein each of the sequences are under the control of a transcriptional promoter, and the activity of the inhibitory transcript is optionally regulated with at least one external agent, and the activity of the transcript of interest is optionally regulated with at least one external agent, and
 - coexpressing said nucleic acids in the target tissue or cell to constitutively inhibit the activity of the transcript of interest with the inhibitory transcript.
2. (Originally Presented) The method according to Claim 1, further comprising administering to the target nonhuman animal tissue or cell at least one external agent which causes the activity of said inhibitory transcript to be inhibited, for the purpose of restoring the activity of the transcript of interest.
3. (Originally Presented) The method according to Claim 2, further comprising administering to the target nonhuman animal tissue or cells at least one external agent which causes the activity of said transcript of interest to be increased, for the purpose of restoring the activity of the transcript of interest.

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4. (Originally Presented) The method according to Claim 1, further comprising administering to the target nonhuman animal tissue or cells at least one external agent which causes the activity of said transcript of interest to be increased, for the purpose of restoring the activity of the transcript of interest.

5. (Originally Presented) The method according to Claim 1, wherein the inhibitory transcript is under the control of a repressible promoter, and at least one external agent causes the inhibition of said promoter.

6. (Originally Presented) The method according to Claim 5, wherein the promoter comprises at least one repeat of the tetracycline response operator, and at least one external agent is an external repressor agent chosen from tetracycline and tetracycline analogues.

7. (Originally Presented) The method according to Claim 1, wherein the nucleic acid encoding the inhibitory transcript also comprises an activatable autocatalytic aptamer sequence, and the method comprises at least one external agent which is a specific ligand of the aptamer and which is an activator of the aptamer.

8. (Withdrawn) The method according to Claim 1, wherein the nucleic acid encoding the inhibitory transcript also comprises a sequence which can be recognized by a ribozyme with ligand-dependent activity, and the external agent is a ligand which is an activator of the catalytic activity of the ribozyme.

9. (Originally Presented) The method according to Claim 1, wherein the sequence encoding the transcript of interest is placed under the control of an inducible promoter, and the method comprises at least one external agent which causes the activation of said promoter.

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10. (Originally Presented) The method according to Claim 9, wherein the inducible promoter comprises a PPAR α response element, and wherein at least one external agent is a PPAR α ligand.

11. (Originally Presented) The method according to Claim 10, wherein the inducible promoter comprises a PPAR α response element, and at least one external agent is a PPAR α ligand chosen from fibrates and fibrate analogues.

12. (Originally Presented) The method according to Claim 9, wherein the inducible promoter comprises a PPAR γ response element, and the method comprises at least one external agent which is a PPAR γ ligand.

13. (Originally Presented) The method according to Claim 12, wherein the inducible promoter comprises a PPAR γ response element, and at least one external agent is a PPAR γ ligand chosen from fatty acids and thiazolidinediones.

14. (Originally Presented) The method according to Claim 1, wherein the inhibitory transcript is in the form of an antisense RNA which is complementary to at least one coding portion of the mRNA of the transgene of interest, and the inhibitory transcript is capable of forming with the at least one coding portion of the mRNA of the transgene of interest a Watson and Crick-type linkage.

15. (Originally Presented) The method according to Claim 1, wherein the inhibitory transcript is in the form of an antisense RNA which is complementary to at least one noncoding portion of the mRNA of the transgene of interest, and the inhibitory transcript is capable of forming with the at least one noncoding portion of the mRNA of the transgene of interest a Watson and Crick-type linkage.

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16. (Originally Presented) The method according to Claim 15, wherein the inhibitory transcript is in the form of an antisense RNA which is complementary to at least one noncoding portion at the 5' end of the mRNA of the transgene of interest, and the inhibitory transcript is capable of forming with the at least one noncoding portion at the 5' end of the mRNA of the transgene of interest a Watson and Crick-type linkage.

17. (Originally Presented) The method according to Claim 15, wherein the antisense RNA is at least 10 ribonucleotides long.

18. (Originally Presented) The method according to Claim 1, wherein the inhibitory transcript is in the form of an RNA capable of forming a triple helix with a portion of the nucleic acid comprising the sequence of the transgene of interest.

19. (Withdrawn) The method according to Claim 1, wherein the inhibitory transcript is in the form of a ribozyme.

20. (Originally Presented) The method according to Claim 1, wherein the transgene of interest encodes a protein of therapeutic interest.

21. (Originally Presented) The method according to Claim 1, wherein the transgene of interest corrects a genetic abnormality or of deficiency.

22. (Originally Presented) The method according to Claim 1, wherein the transgene of interest encodes an activator which is involved in the expression of another gene.

23. (Originally Presented) The method according to Claim 1, wherein the transgene of interest produces a transcript of interest having therapeutic activity.

24. (Originally Presented) The method according to Claim 1, wherein the nucleic acids are carried by a single vector or different vectors.

25. (Originally Presented) The method according to Claim 24, wherein the nucleic acids are carried by the same strand of the same vector.

26. (Originally Presented) The method according to Claim 24, wherein the vector is a plasmid, a cosmid, an artificial chromosome or a nonencapsidated DNA.

27. (Originally Presented) The method according to Claim 24, wherein the vector is a recombinant virus.

28. (Originally Presented) The method according to Claim 27, wherein the recombinant virus is an adenovirus, a retrovirus, a herpesvirus, an adeno-associated virus, a phage or a derivative of these.

29. (Withdrawn) The method according to Claim 24, wherein the vector is a bacterium or parasite.

30. (Originally Presented) The method according to Claim 1, wherein the nucleic acids are introduced into the target tissue or cell using a physical or mechanical method.

31. (Originally Presented) The method according to Claim 30, wherein the nucleic acids are introduced into the target tissue or cell using a physical or mechanical method chosen from injection, ballistic technique, electroporation, sonoporation, exposure to an electrical field, exposure to microwaves, exposure to heat or pressure, or by a combination of these techniques.

32. (Originally Presented) The method according to Claim 30, wherein the nucleic acids are introduced into the target tissue or cell by injection, electrotransfer, or a combination thereof.

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33. (Withdrawn) The method according to Claim 1, wherein the nucleic acids are introduced into the target tissue or cell in a form which is complexed with at least one chemical agent or biochemical agent.

34. (Withdrawn) The method according to Claim 33, wherein the at least one chemical agent or biochemical agent is a cationic protein chosen from histones and protamines.

35. (Withdrawn) The method according to Claim 33, wherein the at least one chemical agent or biochemical agent is a polymer chosen from DEAE-dextran, polyamidoamines, polylysines, polyethyleneimines, polyvinylpyrrolidones or polyvinyl alcohols.

36. (Withdrawn) The method according to Claim 33, wherein the nucleic acids are incorporated into lipids in crude form or in the form of liposomes.

37. (Withdrawn) The method according to Claim 33, wherein the nucleic acids are incorporated into nanoparticles.

38. (Currently Amended) The method according to Claim 1, wherein the target tissue or cell is of nonhuman animal ~~or human~~ origin.

39. (Currently Amended) The method according to Claim 38, wherein said target tissue or cell of nonhuman animal ~~or human origin~~ is a muscle cell or a skeletal muscle tissue.

40. (Withdrawn) The method according to Claim 1, wherein the target tissue or cell is of plant origin.

41. (Originally Presented) The method according to Claim 30, wherein the nucleic acids are injected systemically.

42. (Originally Presented) The method according to Claim 41, wherein the nucleic acids are injected intra-arterially or injected intravenously.

43. (Originally Presented) The method according to Claim 42, wherein the nucleic acids are present in a composition comprising pharmaceutically acceptable excipients for the intra-arterial or intravenous methods of administration.

44. (Originally Presented) The method according to Claim 30, wherein the nucleic acids are administered parenterally, topically, cutaneously, vaginally, intranasally, subcutaneously, intra-ocularly, or a combination thereof.

45. (Originally Presented) The method according to Claim 44, wherein the nucleic acids are present in a composition comprising pharmaceutically acceptable excipients for the parenteral, topical, cutaneous, vaginal, intranasal, subcutaneous or intra-ocular methods of administration.

46. (Withdrawn) A composition comprising a first nucleic acid comprising a sequence of a transgene of interest encoding a transcript of interest, and comprising a second nucleic acid comprising a sequence of an inhibitory transgene encoding an inhibitory transcript specific for said transcript of interest, wherein the sequences are each under the control of a transcriptional promoter, and wherein the activity of the inhibitory transcript is optionally regulated with at least one external agent and the activity of the transcript of interest is optionally regulated with at least one external agent.

47. (Withdrawn) The composition according to Claim 46, wherein the inhibitory transcript is in the form of an antisense RNA which is complementary to at least one coding portion of the mRNA of the transgene of interest, and wherein the

antisense RNA is capable of forming with the at least one coding portion of the mRNA of the transgene of interest a Watson and Crick-type linkage.

48. (Withdrawn) The composition according to Claim 46, wherein the inhibitory transcript is in the form of an antisense RNA which is complementary to at least one noncoding portion of the mRNA of the transgene of interest, and wherein the antisense RNA is capable of forming with the at least one noncoding portion of the mRNA of the transgene of interest a Watson and Crick-type linkage.

49. (Withdrawn) The composition according to Claim 48, wherein the inhibitory transcript is in the form of an antisense RNA which is complementary to at least one 5' noncoding portion of the mRNA of the transgene of interest, and wherein the antisense RNA is capable of forming with the at least one 5' noncoding portion of the mRNA of the transgene of interest a Watson and Crick-type linkage.

50. (Withdrawn) The composition according to Claim 46, wherein the antisense RNA is at least 10 ribonucleotides long.

51. (Withdrawn) The composition according to Claim 46, wherein the inhibitory transcript is in the form of an RNA capable of forming a triple helix with a portion of the nucleic acid comprising the sequence of the transgene of interest.

52. (Withdrawn) The composition according to Claim 46, wherein the inhibitory transcript is in the form of a ribozyme.

53. (Withdrawn) The composition according to Claim 46, wherein the sequence encoding the inhibitory transcript is under the control of a repressible promoter, and wherein at least one external agent causes the inhibition of said promoter.

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54. (Withdrawn) The composition according to Claim 53, wherein the promoter comprises at least one repeat of a tetracycline response operator, and at least one external agent is at least one external repressor agent chosen from tetracycline and tetracycline analogues.

55. (Withdrawn) The composition according to Claim 46, wherein the nucleic acid encoding the inhibitory transcript also comprises an activatable autocatalytic aptamer sequence, and wherein the composition further comprises at least one external agent which is a specific ligand of the aptamer and is an activator of the aptamer.

56. (Withdrawn) The composition according to Claim 46, wherein the nucleic acid encoding the inhibitory transcript also comprises a sequence which can be recognized by a ribozyme with ligand-dependent activity, and wherein the composition further comprises at least one external agent which is a ligand of the ribozyme and is an activator of the catalytic activity of the ribozyme.

57. (Withdrawn) The composition according to Claim 46, wherein the sequence of the transgene of interest encoding the transcript of interest is placed under the control of an inducible promoter, and at least one external agent causes the activation of said promoter.

58. (Withdrawn) The composition according to Claim 57, wherein the inducible promoter comprises a PPAR α response element, and at least one external agent is a PPAR α ligand.

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59. (Withdrawn) The composition according to Claim 58, wherein the inducible promoter comprises a PPAR α response element, and at least one external agent is a PPAR α ligand chosen from fibrates and fibrate analogues.

60. (Withdrawn) The composition according to Claim 57, wherein the inducible promoter comprises a PPAR γ response element, and at least one external agent is a PPAR γ ligand.

61. (Withdrawn) The composition according to Claim 60, wherein the inducible promoter comprises a PPAR γ response element, and at least one external agent is a PPAR γ ligand chosen from fatty acids and thiazolidinediones.

62. (Withdrawn) The composition according to Claim 46, wherein the transgene of interest encodes a protein of therapeutic interest.

63. (Withdrawn) The composition according to Claim 46, wherein the transgene of interest corrects a genetic abnormality or deficiency.

64. (Withdrawn) The composition according to Claim 46, wherein the transgene of interest encodes an activator which is involved in the expression of another gene.

65. (Withdrawn) The composition according to Claim 46, wherein the transgene of interest produces a transcript of interest having therapeutic activity.

66. (Withdrawn) The composition according to Claim 46, wherein the nucleic acids are carried by a single vector or different vectors.

67. (Withdrawn) The composition according to Claim 66, wherein the nucleic acids are carried on the same strand of the same vector.

68. (Withdrawn) The composition according to Claim 66, wherein the vector is a plasmid, a cosmid, an artificial chromosome or a nonencapsidated DNA.

69. (Withdrawn) The composition according to Claim 66, wherein the vector is a recombinant virus.

70. (Withdrawn) The composition according to Claim 69, wherein the vector is a recombinant virus chosen from adenoviruses, retroviruses, herpesviruses, adeno-associated viruses, phages, and derivatives thereof.

71. (Withdrawn) The composition according to Claim 66, wherein the vector is a bacterium or a parasite.

72. (Withdrawn) The composition according to Claim 46, wherein the composition is in a form wherein the nucleic acids can be administered *in vivo* to the target tissue or cell using a physical or mechanical technique.

73. (Withdrawn) The composition according to Claim 72, wherein the composition is in a form wherein the nucleic acids can be administered *in vivo* to the target tissue or cell using a physical or mechanical method chosen from injection, ballistic technique, electroporation, sonoporation, exposure to an electrical field, exposure to microwaves, exposure to heat or pressure, or by a combination of these techniques.

74. (Withdrawn) The composition according to Claim 73, wherein the composition is in a form wherein the nucleic acids can be administered by injection, electrotransfer, or a combination thereof.

75. (Withdrawn) A method for regulating a transgene of interest in a target cell or tissue, comprising the composition as defined in Claim 46.

76. (Withdrawn) The method according to Claim 75, wherein the target cell or tissue is of nonhuman animal origin or human origin.

77. (Withdrawn) The method according to Claim 75, wherein the target cell or tissue is a muscle cell or muscle tissue.

78. (Withdrawn) The method according to Claim 75, wherein the target cell or tissue is of plant origin.

79. (Withdrawn) A pharmaceutical composition comprising the composition according to Claim 46 and a suitable pharmaceutical excipient.

80. (Withdrawn) The pharmaceutical composition according to Claim 80 in a form that can be injected into muscle, injected systemically, injected intra-arterially or injected intravenously.

81. (Withdrawn) The pharmaceutical composition according to Claim 80 in a form that can be administered topically, cutaneously, orally, vaginally, intranasally, subcutaneously or parenterally.

82. (Withdrawn) The pharmaceutical composition according to Claim 80, wherein the excipient is an excipient that can be injected into muscle, injected systemically, injected intra-arterially or injected intravenously, or the excipient can be administered topically, cutaneously, orally, vaginally, intranasally, subcutaneously, or parenterally.

83. - 100. Canceled

101. (Withdrawn) A transgenic animal, wherein the animal carries a first nucleic acid comprising the sequence of a transgene of interest encoding a transcript of interest, and a second nucleic acid comprising the sequence of an inhibitory transgene

encoding an inhibitory transcript specific for the transcript of interest, wherein each of the sequences are under the control of a transcriptional promoter, and the activity of the inhibitory transcript is optionally regulated with at least one external agent, and the activity of the transcript of interest is optionally regulated with at least one external agent.

102. (Withdrawn) The transgenic animal according to Claim 102, wherein the inhibitory transcript is in the form of a genetic antisense RNA, of an RNA capable of forming a triple helix or of a ribozyme.

103. (Withdrawn) The transgenic animal according to Claim 102, wherein the inhibitory transcript is regulated negatively via a repressible promoter, and at least one external agent causes the inhibition of said promoter.

104. (Withdrawn) The transgenic animal according to Claim 102, wherein the inhibitory transcript also comprises an activatable autocatalytic aptamer sequence, and at least one external agent is a specific ligand of the aptamer sequence which is an activator of the aptamer sequence.

105. (Withdrawn) The transgenic animal according to Claim 102, wherein the inhibitory transcript also comprises a sequence which can be recognized by a ribozyme with ligand-dependent activity, and at least one external agent is a ligand of the ribozyme which is an activator of the catalytic activity of the ribozyme.

106. (Withdrawn) The transgenic animal according to Claim 102, wherein the transcript of interest is under the control of an inducible promoter, and at least one external agent causes the activation of said promoter.

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107. (Withdrawn) A transgenic plant, wherein the plant carries a first nucleic acid comprising the sequence of a transgene of interest encoding a transcript of interest, and a second nucleic acid comprising the sequence of an inhibitory transgene encoding an inhibitory transcript specific for said transcript of interest, wherein each of the sequences are under the control of separate transcriptional promoters, and the activity of the inhibitory transcript is optionally regulated with at least one external agent, and the activity of the transcript of interest is optionally regulated with at least one external agent.

108. (Withdrawn) The transgenic plant according to Claim 108, wherein the inhibitory transcript is in the form of a genetic antisense RNA, of an RNA capable of forming a triple helix or of a ribozyme.

109. (Withdrawn) The transgenic plant according to Claim 108, wherein the inhibitory transcript is regulated negatively via a repressible promoter, and at least one external agent causes the inhibition of said promoter.

110. (Withdrawn) The transgenic plant according to Claim 108, wherein the inhibitory transcript also comprises an activatable autocatalytic aptamer sequence, and at least one external agent is a specific ligand of this aptamer sequence.

111. (Withdrawn) The transgenic plant according to Claim 108, wherein the inhibitory transcript also comprises a sequence which can be recognized by a ribozyme with ligand-dependent activity, and at least one external agent is a ligand of the ribozyme which is an activator of the catalytic activity of the ribozyme.

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112. (Withdrawn) The transgenic plant according to Claim 108, wherein the transcript of interest is under the control of an inducible promoter and at least one external agent causes the activation of said promoter.

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